

Update on Acne Vulgaris

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Disclosures

- No relevant conflicts of interest.

Learning Objectives

- Describe the four factors of acne pathogenesis
- Assess lesion morphology and severity
- List acne medications and explain their mechanisms of action
- Design an effective treatment plan
- Counsel patients regarding acne skin care
- Review new acne medications

Prevalence

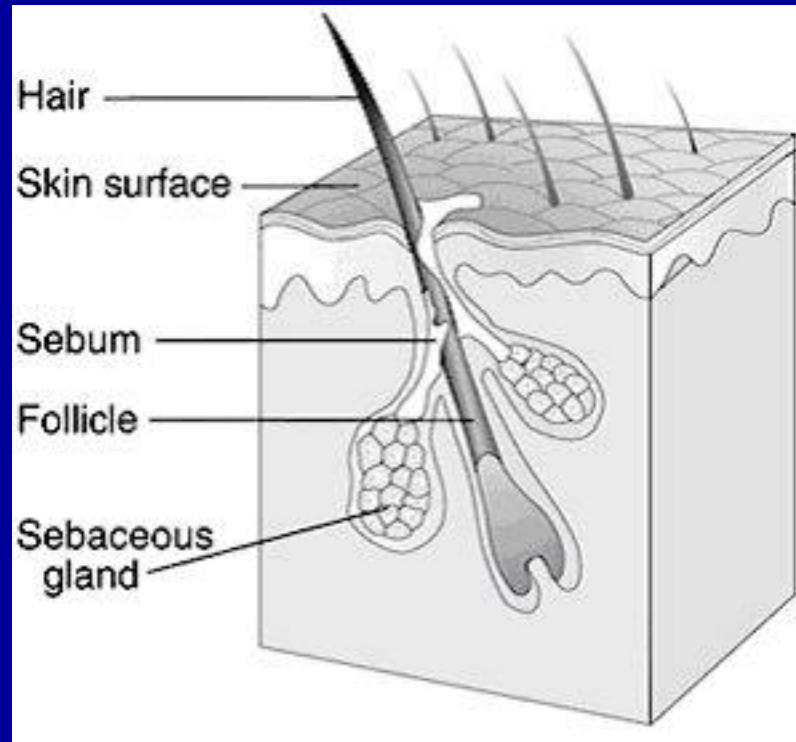
- Extremely common!
 - 80% of adolescents and young adults 11-30 yrs^{1,2}
 - 40-50 million in the United States ³
 - costs exceed \$3 billion per year

Psychosocial Impact

- Negative effects
 - mood, self-esteem, body image ^{4,5}
- Treatment
 - reduces anxiety and depression
 - improves quality of life⁶



Pilosebaceous unit



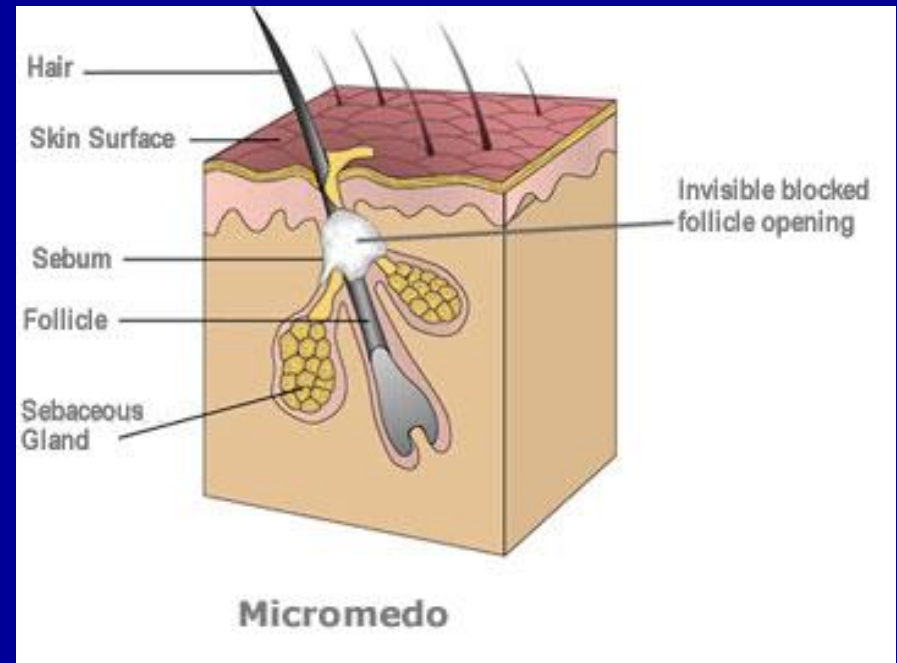
Acne Pathogenesis

Four factors:

1. Sebaceous gland hyperplasia
2. Abnormal follicular desquamation
3. Cutibacterium acnes colonization
4. Inflammation

Acne Pathogenesis

- **Microcomedo**
 - Non-inflammatory comedones
 - Blackhead (open)
 - Whitehead (closed)
 - Inflammatory lesions
 - papules, pustules, nodules, cysts



How to Assess Patient

- Grading systems
 - Help guide therapy and assess response
 - No consensus
- Most combine lesion counting with global assessment of severity⁷

Practical “System”

- **Morphology**
 - Comedonal
 - Inflammatory
 - Mixed
- **Severity**
 - Mild
 - Moderate
 - Severe
- **Sites**
 - Face, chest, back
- **Other**
 - Scarring, PIH, erythema

Severity

Table 1. Classification of Acne.*

Severity	Description
Mild	Comedones (noninflammatory lesions) are the main lesions. Papules and pustules (Fig. 1) may be present but are small and few in number (generally <10).
Moderate	Moderate numbers of papules and pustules (10–40) and comedones (10–40) are present (Fig. 2). Mild disease of the trunk may also be present.
Moderately severe	Numerous papules and pustules are present (40–100), usually with many comedones (40–100) and occasional larger, deeper nodular inflamed lesions (up to 5). Widespread affected areas usually involve the face, chest, and back (Fig. 3).
Severe	Nodulocystic acne and acne conglobata with many large, painful nodular or pustular lesions are present, along with many smaller papules, pustules, and comedones (Fig. 4A).

* The information is from Cunliffe et al.¹²

Noninflammatory lesions



Closed comedones



Open comedones

Inflammatory lesions

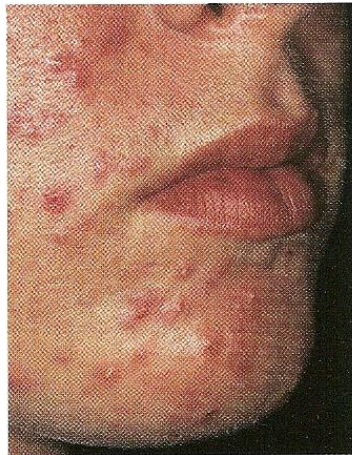


Papules/pustules



Nodules

ACNE CLASSIFICATION AND GRADING



Mild
Papules/pustules +/+
Nodules 0



Moderate
Papules/pustules +++
Nodules +/+



Severe
Papules/pustules +++/
Nodules +++

Treatment

- **TOPICAL**

- OTC

- Benzoyl peroxide
 - Salicylic acid

- Prescription

- Antimicrobials
 - Retinoids
 - Combination products

- **SYSTEMIC**

- Antibiotics

- OCP's

- Isotretinoin

OTC Topicals

- Benzoyl peroxide and Salicylic acid
- Very mild acne
- Salicylic acid less effective than benzoyl peroxide^{8,9}

Benzoyl Peroxide

- MOA
 - kills *C. acnes* ¹⁰
 - mild comedolytic ¹⁰
 - mild anti-inflammatory ^{11, 12}
- Limits development of *C. acnes* antibiotic resistance¹³
- Combine with retinoid to increase efficacy¹⁴
- No resistance reported¹⁵

Benzoyl Peroxide

- “GRASE” by FDA
- Side effects
 - Irritation
 - Bleaching
 - ACD
- Variety of formulations
 - 2.5% to 10%

Topical Antibiotics

- Clindamycin, erythromycin
- MOA
 - Antibacterial¹²
 - Anti-inflammatory¹²
- Side effects
 - Irritation
 - Colitis reported with clindamycin

Topical Antibiotics

- Not recommended as monotherapy
 - Slow onset
 - Resistance
 - Not comedolytic
- Add topical BP or use a combo product
 - BP + clindamycin
 - Benzaclin® gel, Duac® gel
 - BP + erythromycin
 - Benzamycin® gel

Topical Retinoids

- Mechanism of Action
 - Normalize follicular desquamation¹⁶
 - Anti-inflammatory¹⁷
 - Enhance penetration of other compounds¹⁷
- Indications
 - First line therapy for all types of acne
 - Preferred for maintenance therapy^{18,19}
- Side Effects
 - Dryness!
 - Local irritation

Topical Retinoids

- **Adapalene**

- Cream 0.1%
- *Gel 0.1, 0.3%
- Lotion 0.1%

*Differin™ (otc)

- **Tretinoin**

- Cream 0.025, 0.05, 0.1%
- Gel 0.01, 0.025, 0.05%
- Micro 0.04, 0.1 %

* Gel 0.05% (Atralin®)

FDA approved for $\geq$
10 yrs

- **Tazarotene**

- Cream 0.05, 0.1%
- Gel 0.05, 0.1%
- *Pregnancy X

Topical Retinoid Combination Products

- Tretinoin 0.025% + Clindamycin 1.2%
 - Ziana® (FDA approved for ≥ 12 yrs)
 - Addition of BP recommended
 - Generic available
- Adapalene 0.1% + BP 2.5%
 - Epiduo® (FDA approved for ≥ 9 yrs)
 - Generic available
- Adapalene 0.3% + BP 2.5%
 - Epiduo Forte ® (FDA approved for ≥ 12 yrs)
 - Generic available

Topical Retinoid Combination Products

- Pros
 - Qday
- Cons
 - Fixed retinoid (low concentration)
 - \$\$\$ (hundreds for 30-45 gm)

Systemic Antibiotics

- Moderate to severe inflammatory acne
- Most not FDA approved for acne
 - Solodyn® (ER minocycline) at 1 mg/kg/day
 - ≥ 12 yr
 - Seysara® (sarecycline) Oct 2018
 - ≥ 9 yr
 - 30 d of 60 mg= approx. \$1,000
- MOA:
 - Antibacterial
 - Anti-inflammatory
- Goal is 3-4 month course
 - maintenance with topical

Systemic Antibiotics

- Preferred oral antibiotics (for ≥ 8 yrs)
 - *Doxycycline: 50-100 mg po qd-bid
 - Tetracycline: 500 mg po bid
 - Minocycline: 50-100 mg po qd-bid

Systemic Antibiotics

- Generally well-tolerated
- Severe side effects uncommon
 - **Tetracycline:** GI upset, tooth staining (<8 yr)
 - **Doxycycline:** GI upset, photosensitivity, esophagitis
 - **Minocycline:** dyspigmentation, lupus-like reactions, pseudotumor cerebri, SJS, Drug Hypersensitivity

Hormonal Therapy

Combination Oral Contraceptives

- Consider for females with moderate to severe inflammatory/mixed acne
 - FDA approved for 14-15 yr
- MOA: Anti-androgen effects suppress sebum production
- Brands FDA-approved for use in acne:
 - Ortho-Tricyclen® (≥ 15)
 - Yaz® (≥ 14)
 - Estro-Step® (≥ 15)
 - Beyaz® (≥ 14)

Hormonal Therapy

- Potential Side Effects
 - Cardiovascular Risks
 - Venous Thromboembolic Events (VTEs)
 - MI
 - Stroke
 - Cancer: Breast, Cervical
 - Osteopenia
 - Avoid in < 14 yr or within 2 yr of first menses

New Meds

- Amzeeq® (10/2019)
 - Topical minocycline foam 4%
 - ≥ 9 yr
 - 30 gm=\$520
- Twyneo® (7/2021)
 - Encapsulated benzoyl peroxide 3% and tretinoin 0.1%
 - ≥ 9 yr
 - 30 gm=\$457

New Meds

- Aklief® (10/2019)
 - Trifarotene cream 0.005%
 - ≥ 9 yr
 - MOA: retinoic acid receptor agonist, but unclear
 - 45 g=\$683
- Arazlo®
 - Tazarotene lotion 0.045%
 - ≥ 9 yr
 - 45 g=\$512

New Meds

- Winlevi® (8/2020)
 - Clascoterone cream 1%
 - ≥ 12 yr
 - MOA: androgen receptor inhibitor, but unclear
 - 60 g=\$589

Oral Retinoids

- Indications for isotretinoin
 - Severe
 - Scarring
 - Refractory
 - Including moderate cases

Oral Retinoids (cont.)

- Mechanism of Action
 - Decreases size/activity of sebaceous glands
 - Reduces sebum production by >90%
 - Normalizes follicular keratinization
 - prevents new comedones
 - Inhibits *C. acnes*
 - Anti-inflammatory¹⁸

Oral Retinoids (cont.)

- Common side effects
 - dry lips, skin, and eyes
 - nosebleeds
 - mild headaches
 - muscle aches
 - backaches

Oral Retinoids (cont.)

- Potentially serious side effects
 - Teratogenic effects
 - iPledge
 - Depression, suicidal ideation
 - No causal relationship established¹⁹
 - Skeletal changes
 - Fractures, hyperostosis, epiphyseal closure^{20,21}
 - IBD?
 - Data conflicting (UC > CD)²²
 - No causal relationship established

Other Therapies

- Complementary/Alternative
 - Limited data regarding safety and efficacy
 - Herbal compounds
 - Biofeedback
- Chemical peels
 - Glycolic and salicylic acid peels helpful for comedones

Other Therapies

- Lasers and Light
 - Best evidence for Photodynamic Therapy (PDT)
 - Photosensitizer applied
 - Absorbed by sebaceous glands
 - Activated with light
- Intralesional Steroid Injections
 - Nodules
 - Decreased pain and swelling

Simple Treatment Algorithm

- Mild comedonal
 - topical retinoid (or benzoyl peroxide)
- Mild inflammatory/mixed
 - topical retinoid + topical antimicrobial
- Moderate inflammatory/mixed
 - topical retinoid + topical antimicrobial + oral antimicrobial
- Severe inflammatory
 - Minimal scarring: topical retinoid + topical antimicrobial + oral antimicrobial
 - Scarring or multiple treatment failures: Isotretinoin



Mild to moderate comedonal

- Topical retinoid





Mild Mixed Acne

- Topical retinoid + topical antibiotic





Moderate Mixed Acne

Topical retinoid + topical antimicrobial + oral antibiotic



Severe Mixed/Inflammatory Acne



Severe Mixed Acne

- Severe Mixed
 - Minimal scarring: topical retinoid + topical antimicrobial + oral antibiotic
 - More severe scarring: Isotretinoin



Chest/Back Acne



Chest/Back Acne

- Mild
 - Benzoyl peroxide wash
- Moderate
 - Oral antibiotic
- Severe
 - Isotretinoin

Basic Skin Care for Acne

- Gentle cleansing 1-2 times a day
- Mild, fragrance-free cleanser
- Oil-free moisturizer with SPF 30+ bid and prn
- Avoid OTC acne washes and topicals
 - Too irritating/drying

Address Common Acne Myths

- Acne is not caused by poor hygiene or dirt.
- Diet controversial
 - high glycemic index diet may lead to hyperinsulinemia and stimulate androgen synthesis
 - Skim milk²³
 - Nutritional supplements
 - whey

Table 2		
Glycemic Indices and Glycemic Loads of Common Foods		
Food	Glycemic Index	Glycemic Load ^a
White bread	72	10
Whole wheat bread	72	8
Baked potato	111	33
Sweet potato	61	11
Carrots	35	2
Honey	69	15
Watermelon	72	4
Banana	62	16
Grapes	59	11
Apple	39	6
Cranberry juice cocktail	68	24
Yogurt (low fat)	27	9
Skim milk	32	4
Whole milk	41	5

^a Glycemic load = glycemic index × carbohydrate content in 100 g portions. Glucose is used as the reference and has a glycemic index of 100.
Source: References 7, 9.

Diet and Acne

- No specific dietary changes are recommended.
- Supplements?
 - Antioxidants (e.g., zinc)
 - Probiotics
 - Fish Oil

Other Patient Education

- Discourage picking!
 - permanent scarring
- Post-inflammatory hyperpigmentation
- Explain how to use medicines
 - Small amount
- Potential side effects
 - Expect dryness
- Consistent use for 6-8 weeks minimum

When to Refer

- Severe Acne (cysts, nodules, scars)
- No response or poor response to treatment after 12 weeks
- If systemic antibiotics needed >1 year
- Isotretinoin being considered
 - Females will need OCP
- Acne associated with a systemic disease

- For physicians:
 - <http://www.aad.org/dermatology-a-to-z/diseases-and-treatments/a---d/acne>
 - <http://www.pedsderm.net/webinars/acne-module.html>
 - <http://www.acneandrosacea.org>
 - https://pedsderm.net/site/assets/files/1028/1_spd_acne_s hort_web_final.pdf
- For patients:
 - <http://www.aad.org/dermatology-a-to-z/for-kids>

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